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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/075,335 | 02/14/2002 | Stephen D. Ginsberg | HO-P02202US2 | 8704 |
| 27123 | 7590 | 06/10/2005 | EXAMINER | |
| MORGAN & FINNEGAN, L.L.P. 3 WORLD FINANCIAL CENTER NEW YORK, NY 10281-2101 | | | HORLICK, KENNETH R | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1637 | |

DATE MAILED: 06/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/075,335

Applicant(s)

GINSBURG ET AL.

Examiner

Kenneth R. Horlick

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 59-62 and 80-115 is/are pending in the application.
- 4a) Of the above claim(s) 59-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 80-115 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

1. The title of the invention is still not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. "RNA amplification methods using a terminal continuation oligonucleotide and transcriptional promoter sequence" is suggested.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 80-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik et al. (US 5,962,272) in view of Van Gelder et al. (US 5,545,522).

These claims are drawn to a method of RNA amplification, comprising incubating a target strand with a synthesis primer and a terminal continuation oligonucleotide, wherein at least one of the terminal continuation oligonucleotide or the primer comprises

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a transcriptional promoter sequence; extending the primer to form a first strand cDNA; incubating the first strand cDNA with the terminal continuation oligonucleotide; extending said oligonucleotide to form a second strand cDNA; incubating the cDNA with an RNA polymerase; and transcribing a plurality of RNA transcripts from the cDNA.

Chenchik et al. disclose a method of RNA amplification using a synthesis primer and a terminal continuation oligonucleotide (called a "CapSwitch" oligonucleotide), wherein the amplification product is double-stranded DNA (see especially Fig. 3-1 and columns 2-13). With respect to both said oligonucleotide and primer, Chenchik et al. disclose numerous modifications, including incorporation of RNA polymerase promoter sequences (column 6, lines 6-34 and column 10, lines 20-44).

While Chenchik et al. disclose modification of their basic method using oligonucleotides and/or primers comprising a transcriptional promoter sequence, they do not explicitly disclose the use of these sequences to form a plurality of RNA transcripts from the synthesized double-stranded cDNA. That is, the patent notes that such modifications "...simplify subsequent purification, using and cloning cDNA...".

Van Gelder et al. disclose the incorporation of a transcriptional promoter sequence on a primer for extending a target RNA sequence into a cDNA, wherein said sequence advantageously provides for synthesis of a plurality of RNA transcripts from the cDNA using an RNA polymerase (see Figure 1 and columns 2-10).

One of ordinary skill in the art would have been motivated to use the embodiment of Chenchik et al. wherein one or both of the terminal continuation oligonucleotide and the synthesis primer comprise a transcriptional promoter sequence, to form a plurality of

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RNA transcripts from double-stranded cDNA, because Van Gelder et al. disclosed the advantageous use of such promoter sequences for that purpose. In other words, given the teachings of Van Gelder et al., the claimed method would have been an obvious and suggested extension or application of the method of Chenchik et al., providing the expected benefit of amplified RNA from the cDNA. Regarding the dependent claims, these indisputably relate to well known, conventional methodologies and parameters in nucleic acid manipulation and histology, and thus clearly do not bear on patentability. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods.

3. With respect to the above rejection, the arguments of the response filed 04/05/05 have been fully considered, but are not found persuasive. The response argues that there is no motivation or guidance in the cited art to carry out the claimed methods, and that the rejection relies on improper hindsight. The response also requests that the Office specifically point out in Van Gelder the alleged motivation to combine or modify the Chenchik and Van Gelder methods to result in a method of amplifying RNA using two primers, a terminal continuation oligonucleotide and synthesis primer as claimed in the present invention.

It is submitted that motivation to support a proper case of *prima facie* obviousness has been provided in the rejection, and that the arguments of the response are directed to the references individually rather than their combined teachings as a whole. In short, the rejection argues that the claimed methods are a straightforward

combination of the use of a "CapSwitch" or terminal continuation oligonucleotide (as disclosed by Chenchik et al.) and a cDNA synthesis primer comprising a transcriptional promoter sequence for facilitating the amplification of RNA (as disclosed by Van Gelder et al.). Importantly, as pointed out in the rejection Chenchik et al. taught the benefit of including an RNA polymerase promoter sequence on either or both of their "CapSwitch" oligonucleotide and synthesis primer. However, as also pointed out in the rejection, Chenchik et al. do not teach all possible applications of the use of such promoter sequences, particularly as a means of facilitating amplification of RNA from a cDNA template. Van Gelder et al. has been cited because it clearly discloses the use of a cDNA synthesis primer comprising an RNA polymerase promoter sequence as an advantageous means of facilitating amplification of RNA from a cDNA template (Fig. 1). Thus, one of ordinary skill in the art would have been motivated to use the promoter sequence-containing synthesis primer of Van Gelder et al. in the method of Chenchik et al. because this would have provided the expected advantage that the cDNA product of Chenchik et al. would have the additional benefit of enabling synthesis of amplified RNA for further use in any number of applications (e.g., use as a probe). The rejection is still believed to be proper and is therefore maintained.

4. No claims are free of the prior art.


5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kenneth R Horlick whose telephone number is 571-272-0784. The examiner can normally be reached on Monday-Thursday 6:30AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Kenneth R Horlick
Primary Examiner
Art Unit 1637

06/01/05